Species	N	MIC (mg/L) required to inhibit % strains					
		Teicoplanin			Vancomycin		
		50%	90%	100%	50%	90%	100%
S. aureus	428	1	4	8	1	2	4
all Coag -ve Staph.	191	2	8	16	2	2	4
S. epidermidis	124	2	8	16	2	2	4
S. haemolyticus	29	2	8	16	2	2	4
Streptococcus spp	34	≤ 0.125	1	4	1	2	4
Enterococcus spp	323	0.25	1	64	2	4	64
E. faecalis	208	0.25	0.5	64	2	4	64
E. faecium	47	0.5	2	64	1	2	64

On the basis of MIC_{90} criteria, vancomycin was 2–4 times more active than teicoplanin against staphylococci whereas teicoplanin was at least two fold more active against streptococci. Teicoplanin was generally four to eight fold more active than vancomycin against the majority of *Enterococcus* spp. The incidence of enterococci resistant to teicoplanin (0.62%) and vancomycin (0.93%) was low.

P730 Activity of Teicoplanin, Vancomycin and 8 Other Drugs Against Gram-Positive Pathogens Isolated in Italy

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At present only the glycopeptides teicoplanin and vancomycin retain, in most sites, a consistent activity against multi-drug resistant Gram-positive pathogens responsible for serious infections in the community and in nosocomial settings. Thus, monitoring their continuous efficacy becomes essential since the clinicians are accustomed to use these drugs on an empirical basis. In 1995 a large multicenter study enrolling 70 laboratories in 9 European countries has analysed 6824 Gram-positive isolates for susceptibility to the two glycopeptides. In Italy, besides teicoplanin and vancomycin, the *in vitro* activity of several other relevant drugs was assessed by an agar dilution method (NCCLS) on the collection of strains (807) sent to this coordinating laboratory. Percent susceptible organisms at the breakpoints (NCCLS, 1995) are reported in the table for the antibiotics tested:

Pathogen		% Susceptible organisms to									
	n	amp	pen	cef	imi	net	ery	nor	cip	tei	van
Staph. (MS)	280		32.5	100	100	95	51	75	69	100	100
Staph. (MR)	219					80	10	14	10	99.6	100
E. faecalis	247	87			94			66	42	99.6	99.6
E. faecium	46	28			43			52	17	100	98

This survey confirms that teicoplanin is more active than vancomycin on Enterococci and that it displays in practice comparable potency against the Staphylococci. In accordance with the data obtained in other countries it may be concluded that usage of the two glycopeptides, as occurring in Europe, may delay the appearance and spread of glycopeptide-resistant Gram-positive pathogens as experienced in other regions of the world where only one molecule is employed. One possible mechanism for this may be ascribed to the fact that vancomycin can easily induce organisms carrying the VanB phenotype to full blown resistance while teicoplanin is devoid of this untoward effect.

Epidemiology of antibiotic resistance II

P731 Emergence of Fluoroquinolone Resistance in Central Europe

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Objectives: To evaluate the influence of an increasing consumption of fluoroquinolones on the prevalence of fluoroquinolone resistance in clinical isolates of frequently encountered bacterial species.

Methods: The susceptibility data from 4 collaborative studies (each comprising more than 20 centres) conducted in 1983 (prior to the introduction of any fluoroquinolone), 1986 (after introduction of norfloxacin and ofloxacin in Germany), 1990 (after introduction of ciprofloxacin in Germany), and 1995 were analyzed. Uniform standard methods for identification of the bacteria and susceptibility testing were used. MICs were determined by the broth microdilution method. A total of 14,960 strains were under investigation. Data are presented for ciprofloxacin regarded as a representative fluoroquinolone.

Results: Considering ≥4 mg/l as a breakpoint for resistance to ciprofloxacin the incidence of resistant strains of *Enterobacteriaceae* remained below 1% until 1990, but increased to 3.8% (*E. coli* 5.2%) in 1995. The resistance rates in *P. aeruginosa* were 0.7%, 1%, 6.4%, and 11.9%, in *S. aureus* 0%, 0.5%, 6.2%, and 12.8%, and in *E. faecalis* 2.2%, 0.7%, 7.7%, and 28.9%. The resistance rate in CNS increased from 19.6% (1990) to 44.5% (1995). In the latest study *E. faecium, MRSA,* and *MR-CNS* had the highest resistance rates (73.1%, 89.6% and 69.8%, respectively).

Conclusions: The increasing consumption of fluoroqinolones seems to select resistant populations. Fluoroquinolone resistance has emerged in Central Europe.

P732 Multicenter Survey of *Escherichia coli* Resistant to Ciprofloxacin: Analysis of Clonal Diversity and Gyrase Mutation

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Objectives: To determine the rate of ciprofloxacin (CIP) resistance by using the ATB system in *E. coli* isolates collected from two multicenter surveys of 11 Belgian hospitals and to define clonal diversity and gyrase mutation in CIP-*E. coli* isolates.

Methods: CIP-R isolates were analysed by genomic typing (Arbitrary Primer-PCR analysis using ERIC1R and ERIC2 primers and PFGE analysis using *XbaI*). Detection of *gyrA* codon 83 mutation was done by using PCR amplification of the *gyrA* QRDR region and *HinfI* RFLP analysis.

Results: The rate of CIP-R in *E. coli* isolates increased from 12/520 (2%) in 1991 to 27/504 (5%) in 1993 ($p < 0.01$). CIP MICs ranged from 4 to 64 μg/ml. AP-PCR analysis discriminated 14 genotypes and PFGE typing delineated 15 major types among 23 available CIP-R isolates from 1993 survey. Genotypes appeared geographically dispersed. All CIP-R isolates exhibited the most frequently reported mutation in codon 83 of *gyrA*.

Conclusions: These data indicate that CIP resistance is increasing among *E. coli* isolates from hospitalized patients in Belgium. Genomic diversity suggests that polyclonal emergence of CIP-R mutants is the predominant mechanism. Although a common *gyrA* mutation was found in CIP-R strains, the presence of additional mutations in *gyrA* and/or *parC* genes may explain the high resistance displayed by the majority of strains.

P733 Accumulation of Fluoroquinolones (FQ) in *Acinetobacter baumannii* (Ab)

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Objectives: To evaluate the relationship between accumulation and activity of FQ in clonally non-related clinical isolates of Ab.

Methods: Six strains of Ab corresponding to different pulse-field gel electrophoresis types were used. MICs of norfloxacin (NOR) and pefloxacin (PFX) were determined by microdilution (NCCLS). Two sets of 500 μL of cells in PBS (4°C; 1.5 A_{550} U/ml) and FQ (10 mg/L) were incubated with shaking for 10 min at 37°C. Cells (500 μL) from the first set were added to a new tube containing 500 μL of silicon oil (ρ: 1.029); the second set of tubes was washed twice with 1-mL of cold PBS. Cells were collected by centrifugation. Two mL of 0.1M glycine-HCl (pH 3.0) were added to each pellet; cells were disrupted by vortexing and overnight incubation (25°C). Cell debris was removed by centrifugation (4°C, 13,000 rpm, 5 min) and the amount of FQ was determined by fluorescence emission of the supernatant at 445 nm (NOR) or 441 nm (PFX).

Results: MICs (mg/L) and accumulation (ng/mg dry weight of cells) were:

		Strain					
		12	104	30	14	32	55
NOR	MIC	1024	64	64	64	4	4
	ACCUM.	279 ± 6	349 ± 24	287 ± 17	429 ± 17	267 ± 40	385 ± 20
PFX	MIC	64	16	8	4	0.25	0.125
	ACCUM.	297 ± 45	449 ± 54	225 ± 12	410 ± 13	291 ± 44	237 ± 20

In assays without silicon oil, lower values of accumulation were obtained.

Conclusions: The activity of NOR and PFX against Ab is not directely related to the degree of accumulation of these drugs in the organism.

P734 Ciprofloxacin Resistant *Campylobacter* Species in Styria, Austria

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Objectives: *Salmonella* and *Campylobacter* species are the most significant diarrhea-causing pathogens in our region. In 1996 about 30.000 stool specimen were tested in the three most important bacteriological laboratorys in Styria (Austria). The mean isolation rate of *Campylobacter jejuni/coli* was 2.18%. 653 isolates from 571 patients were found. Distribution of these isolates shows a high prevalence in the age group from 0–10 years.

Method: To evaluate the ciprofloxacin resistance all isolates were tested routinely with agar diffusion, 100 strains were additionally tested by the E-test.

Result: The ciprofloxacin resistance rate was 25.2%. The distribution in the different age groups shows no significant difference.

Conclusion: Empirical therapy of *Campylobacter* infection with ciprofloxacin is not justified in our region. The high rate of ciprofloxacin resistance requires a routine susceptibility testing, also to verify further resistance development. The antibiotic of choice remains erythromycin with a still low resistance rate (1.4%). The use of enrofloxacin in veterinary medicine should be handled restrictively.

P735 Characterization of Quinolone-Resistant Clinical Isolates of *Citrobacter freundii*

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Objective: The quinolone-resistance mechanisms are classified into three major categories: Target mutations, permeability alterations or overexpression of efflux pumps. The aim of this study was to establish which of these mechanisms were present in four quinolone-resistant clinical isolates of *Citrobacter freundii*.

Methods: Eight clinical isolates of *Citrobacter freundii* with a range of ciprofloxacin MIC from ≤0.007 to 32 μg/ml and ≤2 to >1024 μg/ml for nalidixic acid were chosen.

Using conserved amino acid sequence motifs found in several GyrA and ParC proteins, two sets of primers were designed. The PCR products were recovered and directly sequenced.

Results: All the resistant strains showed a high nalidixic acid resistance level (MIC ≥ 1024 μg/ml) No mutations were observed in the *gyr*A and *par*C genes of the four quinolone susceptible strains, whereas all the quinolone resistant strains showed mutations in these genes. Three of these strains (ciprofloxacin MIC 8–32 μg/ml) showed a concomitant mutation Ser-83 to Ile and Asp-87 to Tyr in GyrA and Ser-80 to Ile in ParC. The fourth (ciprofloxacin MIC 16 μg/ml) showed a mutation Ser-83 to Ile in the GyrA and Ser-80 to Ile in ParC.

Conclusion: Mutations in *gyr*A and *par*C genes plays an important role in the acquisition of quinolone resistance in clinical isolates of *Citrobacter freundii*.

P736 Molecular Analysis of Quinolone Resistance in Worldwide Isolates of *Acinetobacter baumannii*

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Objective: To determine the molecular basis of resistance to quinolones in *Acinetobacter baumannii* isolates from various countries of the world.

Methods: Quinolone resistance in bacteria has been associated with specific mutations in the *gyrA* and *parC* genes. To determine whether such mutations are common in *A. baumannii*, 12 resistant clinical isolates (MICs of nalidixic acid, 256–>1024 mg/L: ciprofloxacin, 1–64 mg/L) from 8 different countries were first characterised by biotyping, tDNA fingerprinting and random-primed (RAPD) fingerprinting. Conserved regions encompassing the active sites of the *gyrA* and *parC* genes were then amplified by PCR and analysed by restriction endonuclease digestion and DNA sequencing.

Results: RAPD fingerprinting demonstrated that the 12 isolates were genetically unrelated. PCR amplification yielded 342-bp and 327-bp products, respectively, from the conserved *gyrA* and *parC* regions of each strain. *Hin*fI digestion of the amplified regions from quinolone-sensitive strains yielded two fragments in each case because of *Hin*fI restriction sites at Asp82-Ser83 in *gyrA* and Asp79-Ser80 in *parC*. All 12 resistant isolates had lost the *Hin*fI restriction site in *gyrA*, in most cases following a mutation of Ser83 to Leu. Five of the 12 isolates also had a mutation at Ser80 in the conserved region of *parC*.

Conclusions: Highly similar mutations to quinolone resistance occur in unrelated strains of *A. baumannii* isolated worldwide. All resistant isolates examined had mutations in the *gyrA* gene, but secondary mutations in the *parC* gene were found in isolates with the highest quinolone MICs.

P737 Emergence of Resistant *Pseudomonas aeruginosa* during Imipenem (IMP) vs Piperacillin-Tazobactam (P/T) Therapy

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Objectives: To compare the rates of emergence of resistant *Pseudomonas aeruginosa* (*Pa*) in patients (pts) treated with IMP or with P/T.

Methods: Case-control study nested in a randomized clinical trial of P/T 4.5 g tid vs IMP 0.5 g qid to treat 313 pts with nosocomial pneumonia or acute peritonitis. Cases were pts with *Pa* susceptible to both drugs at randomization (disk-diffusion testing) and subsequent clinical detection of *Pa* resistant to the drug they were on (same culture site). Controls were pts with susceptible *Pa* at randomization and with lack of subsequent resistant isolates. Univariate and multivariate (logistic regression) analyses were performed.

Results: 13 cases and 40 controls were identified. In univariate analysis, exposure to IMP resulted more often in detection of resistant *Pa* than exposure to P/T (11/28, 39% vs 2/25, 8%) (Odds Ratio = 7.4, p = 0.01). The APACHE II scores were higher in cases than in controls (p = 0.09). No significant difference was found between cases and controls for sex, age, weight, disease (pneumonia vs peritonitis), days of treatment, days of mechanical ventilation, prior surgical procedures, prior antibiotic treatments, and bacteremic or polymicrobial infections. Pts on IMP had not been cultured significantly more often than pts on P/T. Multivariate analysis confirmed the difference in antibiotic exposures while controlling for APACHE II scores (OR = 6.3, p = 0.03).

Conclusions: Resistant *P. aeruginosa* (whether same or new strains) emerged more often during IMP therapy than during P/T therapy. Since no systematic surveillance was performed, the rates might be higher for both drugs.

P738 Evolution of the Antimicrobial Resistance in *Haemophilus spp* in a Five Years Period

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Objectives: To analize the antimicrobial resistance in *Haemophilus spp.* isolates during a five years period.

Methods: From January, 1991 to March, 1995 we registered in our department a total of 1004 Haemphilus isolates obtained from clinical samples. The isolation site frequencies were, 45% from respiratory tract, 25% from conjunctival swabs, 10% from otical swabs, 6% from blood and 14% from other sources. Antimicrobial susceptibility was determined for 10 antimicrobials according to NCCLS recommendations. Antimicrobials assayed were: ampicillin (AMP), amoxicillin/clavulanate (AMC), cefotaxime (CTX), imipenem (IMP), erythromycin (ERY), azithromycin (AZI), cotrimoxazole (SXT), rifampin (RIF), ciprofloxacin (CIP) and chloramphenicol (CHL).

Results: Beta-lactamase producer strains predominated in blood (47%) and otical and conjunctival swabs (44% and 37%) and were less frequent in respiratory tract (25%) and other sites of isolation (17%). Table shows resistance evolution (in %) for all isolates:

Year	Strains	AMP	AMC	CTX	IMP	ERY	AZI	SXT	CIP
1991	241	36	3	0.8	–	37	–	75	–
1992	264	32	0.7	0	0	53	–	67	0
1993	222	36	3.5	0.9	0.9	81	4	53	2
1994	173	29	1	0.5	0.5	92	0.5	46	1
1995	104	36	3	0	0	96	2	52	1

Conclusions: Antimicrobial resistance *Haemophilus spp.* showed no significant variation during the study period, with the exception of ERY which showed an increasing trend and SXT and RIF with a decreasing trend. We also remark the emergence of strains resistant to CTX, IMP and CIP during this period.

P739 Characterization of *Neisseria meningitidis* Strains Isolated from Cerebrospinal Fluid of Meningitis Patient in Poland During the Last Two Years

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Epidemiological data concerning *N. meningitis* infections have been collected in Poland since 1970. Regular bacteriological monitoring of meningitis cases causes by *N. meningitidis* started in Poland two years ago, due to EMGM cooperation. Thirty one meningococcal strains isolates were collected in 1995 (20% registered cases) and 66 in 1996 (47% registered cases) respectively. All together strains were isolated from cerebrospinal fluid taken from meningitis patients hospitalised in 54 units located in 33 out of 49 districts of Poland. Most of the patients were below 2 years old (43% below 1 year). The predominant meningococcal serogroup was -B (79.3% of all isolates), then serogroups C (12.6%), W-135 (3.5%), and A (2.3%). Only two isolates were notgrupable. Most (59.4%) of the isolates B group and two C were typable by monoclonal antibody "22", recently prepared in Czechs NRL for Meningococcal Infections. These results indicate the epidemiological and clinical significance of new serotype "22" in Central Europe countries. Two isolates of phenotype *N. merlingitidis* C:2a:P1.2, 5, sulphonamide sensitive, which cause epidemic in Czech Republic in 1993, were isolated in the South of Poland recently. The most frequent phenotype found in the last two years in Poland was *N. meningitidis* B:22:NST. Sensitivity of strains to selected antimicrobial agents was also examined. No penicillin resistant strain (MIC >1.0 mg/L) was found among Polish isolates. All strains were susceptible to ciprofloxacin (MIC $\leq$0.016 mg/L), cefotaxime (MIC $\leq$0.04 mg/L), rifampicin (MIC $\leq$0.06 mg/L), tetracycline (MIC $\leq$0.5 mg/L) and chloramphenicol (MIC $\leq$2.0 mg/L). Some strains were resistant to sulphametoxazole (57.6% – MIC = 32 mg/L and 14.2% – MIC = 128 mg/L) what is assumed to be associated with widely distribution of this antimicrobial agent in Poland.

P740 Increasing Antibiotics Resistance in Clinical Isolates of *Haemophilus influenze* in Taiwan

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Objectives: To determine the prevalence of antimicrobial resistance of *H. influenzae* isolated from Taiwan (1994~1995)

Methods: 300 clinical isolates of *H. influenzae* obtained from 10 hospitals throughout Taiwan during June 1994 to April 1995 were examined for, serotype, β-lactamase production and antibiotic susceptibility test (NCCLS microdilution broth method)

Results: Twenty three strains (7.7%) were type b. The remainder were nontypable. The overall rate of β-lactamase production was 57.3% (172/300). Among 128 β-lactamase-negative *H. influenzae* isolates, 30 (10%) were resistant to ampicillin. The resistant rates to ampicillin, trimethoprim-sulfamethoxazole, chloramphenicol, tetracycline, and azithromycin, were 67.3%, 34.3%, 20.3% 27%, and 44.3%, respectively. In contrast, the second and third generation cephalosporins and ciprofloxacin remained active against *H.*

influenzae. A significant number of strains were resistant to multiple antibiotics: 10.7% to three antibiotics (ampicillin, chloramphenicol, and tetracycline) and 5.3% to four antibiotics (ampicillin, chloramphenicol, tetracycline, and trimethoprim-sulfamethoxazole).

Conclusions: There was a significant increase of ampicillin resistance and β lactamase production compared to a previous survey in Taiwan conducted nine years ago. The prevalence of non-β-lactamase-mediated ampicillin resistance (10%) and multiple resistance was markedly high.

P741 Effect of a New Monobactam on the Human Intestinal Microflora and the Occurrence of Beta-Lactamase Activity in Faeces

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Objectives: To evaluate the effect of a new monobactam on the human intestinal microflora, the beta-lactamase activity and the concentration of the antibiotic in faeces before, during and after treatment.

Methods: Faecal samples from 31 healthy volunteers divided in four groups, each group receiving different doses of a new monobactam, were investigated. Doses of 250 mg (group 1; n = 8), 500 mg (group 2; n = 8), 1000 mg (group 3; n = 8) and 2000 mg (group 4; n = 7) administered intravenously were given every 6 hours for 7 days. Stool samples were collected at days 0, 3, 5, 7, 14 and 21.

Results: Administration of the monobactam resulted in a decrease of *E. coli* and other enterobacteria and overgrowth of enterococci. *Clostridium difficile* was found in six persons. In 14 of the 31 volunteers concentrations of monobactam could be detected in faeces during treatment. When the substance was detected, this finding was correlated with a decrease in the number of *Bacteroides* sp. Beta-lactamase was found in almost all samples. The peak of beta-lactamase activity occurred after the peak level of monobactam and was correlated with growth of *Bacteroides* sp., and it is likely that the main beta-lactamase producers are *Bacteroides* sp.

Conclusions: The administration of the new monobactam caused disturbances in the intestinal microflora and beta-lactamase producing bacteria were selected or induced during the treatment. The beta-lactamase producers belonged to *Bacteroides* sp.

P742 Antimicrobial Susceptibility of Invasive Isolates of H. Influenzae (Hi), N. Meningitidis (Nm) and S. Pneumoniae (Sp) in Slovenia

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Background: The increasing antimicrobial resistance of these pathogens provided the rationale for a surveillance study evaluating the prevalence of resistant strains in Slovenia.

Methods: Sp, Nm and Hi isolates from children aged 0–14 years, recovered from normally sterile body sites from 1993 to 1995 were tested for susceptibility to antibiotics. Sp and Hi isolates were evaluated using NCCLS disk diffusion methods. All Sp strains showing reduced susceptibility to penicillin on screening with a 1 μg oxacillin disk were evaluated by the E test for resistance to penicillin, cefotaxime (CFX) and ceftriaxone (CTX). Antimicrobial susceptibility of Nm strains was evaluated by the disk diffusion method.

Results: Fifty-two Sp strains, 52 Hi strains and 33 Nm strains were tested. Of the 52 Sp strains, 19% showed intermediate resistance to penicillin, all were sensitive to CFX, CTX and cefuroxime, and 96% were sensitive to chloramphenicol. Of the 52 Hi strains, 8 (15.3%) were betalactamase positive, and 98% were susceptible to chloramphenicol, 98% to CFX, 92% to CTX, and 96% to cefuroxime. Of the 33 Nm strains tested, 1 (3%) was resistant to penicillin, 1 to cefuroxime and 1 to CTX, but all were susceptible to CFX, chloramphenicol and ampicillin.

Conclusion: CFX without vancomycin ± ampicillin at extremes of age is a rational treatment of community-acquired meningitis. Other invasive infections caused by Sp, Hi and Nm can be treated by cefuroxime as well.

P743 *Escherichia coli* Resistance to Amoxicillin and Co-Amoxiclav in a Community with High Aminopenicillins Consumption Rate

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The antimicrobial susceptibility, following NCCLS methodology, to 96 *E. coli* strains isolated from 94 patients with complicated intra-abdominal infections (colectomy, appendicectomy, gastrectomy, laparotomy and cholecystectomy) or urinary tract infections (UTI) acquired in surgical wards, to amoxicillin, co-amoxiclav (2:1), cefuroxime and cefotaxime was performed during the period March–November 1994.

The distribution of isolates with respect to the source of infection were: appendix (35.5%), bladder (17.25%), caecum/colon/rectum (10.8%), lower UTI (16.1%), pyelonephritis (1.1%) and others (10.8%). According to the type of sample distribution was as follows: peritoneal fluid (58.1%), abcess material (22.6%), urine (16.1%) and others (3.2%).

Using NCCLS breakpoints (1993), 43.8% of strains were susceptible to amoxicillin, 89.6% to co-amoxiclav, 93.8%, to cefuroxime and 100.0% to cefotaxime. Of 15 strains coming from UTI, only one showed an MIC of 32 mcg/ml against co-amoxiclav.

The high amoxicillin resistance rate of these strains is significantly reduced when clavulanate is added to the susceptibility test. The co-amoxiclav resistance rate (4.2%) obtained in our country is similar to the one obtained in other European centers, even though Spain has one of the highest *E. coli* aminopenicillins resistance rates in the European Union.

P744 Antibiotic Consumption Associated with the Prevalence of Antimicrobial Resistance among Clinical Isolates of *E. coli*

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Objectives: The relation between antibiotic consumption and prevalence of antimicrobial resistance was examined for clinical isolates of *Escherichia coli* from 16 departments at a university hospital.

Methods: The resistance patterns of all clinical isolates of *E. coli* from 16 departments at Odense University Hospital, Denmark, were registered during a 6 year period (1987–1992). 7861 isolates from the patients third day of hospitalization or later were included in this analysis. Antibiotic usage was expressed as Defined Daily Doses per 100 bed days.

At department level stepwise multivariable weighted regression analysis was used to correlate the prevalence of resistance to the antibiotic usage and to the patients mean duration of hospitalization.

Results: When the departments were compared, the prevalence of resistance against *commonly* used antibiotics was positively associated with the usage of the antibiotic in question. The prevalence of

resistance against *rarely* used antibiotics was not associated with the usage of the antibiotic in question, but was instead positively associated with the summed usage of the other antibiotics and the patients mean duration of hospitalization at the department.

Conclusion: Differences in the prevalence of antimicrobial resistance of *E. coli* among hospital departments were associated with the antibiotic consumption and the patients mean length of stay at the departments.

P745 Antimicrobial Resistance of *Shigella flexneri* and *Shigella sonnei* in Hong Kong 1986–1995

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Objectives: To examine the change in patterns of antimicrobial resistance to 19 antibiotics of *S. flexneri* and *S. sonnei* in the past decade.

Methods: We studied 334 *S. flexneri* and *S. sonnei* isolated during 1986 to 1995. The MICs of ampicillin (AMP), amoxycillin with clavulanic acid (AMC), piperacillin (PIP), imipenem (IMI), cefepime (CPM), cefotaxime (CFX), ceftazidime (CTZ), cefuroxime (CXM), amikacin (A), gentamicin (G), netilmicin (N), nalidixic acid (Nx), ciprofloxacin (CIP), ofloxacin (OFL), sparfloxacin (SPA), tetracycline (T), chloramphenicol (C), trimethoprim (Tm) and sulphamethoxazole (Sm) were determined by the agar dilution method. The presence of the most common Ser-83 mutation in the gyrase A gene was determined by a previously described PCR method.

Results: Of the 223 1986–95 *S. flexneri* isolates, there was a significant increase in the MICs of all antibiotics tested. Isolates with Nx MICs $\geq$32 mg/L accounted for 57% (55/94) of 1994–5 collection. All showed gyrase mutation. Their MICs of T, Tm, Sm, C, G, IMI, CPM, AMC were significantly higher than those of contemporaries without the gyrase mutation. Of the 111 1986–1995 *S. sonnei* isolates, there was a significant increase in the MICs of CPM, CTX, CTZ, IMI, Nx, CIP, OFL, SPX, Sm and Tm. By 1995, the MICs of all antibiotics of *S. flexneri* were significantly higher than those of *S. sonnei*, with the exception of Sm.

Conclusion: In the past decade, Hong Kong isolates of *S. flexneri* and *S. sonnei* have shown a significant increase in their MICs of antimicrobial agents some of which have not been commonly used for gastroenteritis.

P746 *Pseudomonas aeruginosa* – Trends in Antibiotic Resistance in Bratislava Hospitals

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Nosocomial infections caused by *P. aeruginosa* have been a major problem in hospitalized patients. Our study presents the occurence of antibiotic resistance of *P. aeruginosa* isolates from 6 Bratislava hospitals, mainly from ICUs, Urology, Paediatry and Surgery Departments in the period 1991–1996. Amikacin resistance increased from 4.0% in 1991 to 28% in 1996. Ceftazidime resistance was 1.4% in 1992 and 23% in 1996. With ciprofloxacin an increase from 2.3% resistance in 1991 to 35% in 1996 was observed. The highest rate of resistance was found in strains isolated from urine. In 1996, resistance to meropenem was 40%, piperacillin/tazobactam 20%, azlocilin 40%, tobramycin 43%, ofloxacin 45%, netilmicin 53% and cefotaxime 62%. We observed the frequent occurrence of serogroup 011, which is often associated with the multiple resistance. Mechanisms of such resistance to aminoglycosides was due to the production of aminoglycoside modifying enzymes (AAC (6′)-I and APH (2″)), to beta-lactams was caused by beta-lactamases. Several strains showed impermeability. Its evident that resistance of *P. aeruginosa* strains to a wide spectrum antibiotics increased considerably.

P747 Antibiotic Susceptibilities of Gram-Negative Rods from Blood or CSF

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Objectives: To monitor resistance trends.

Methods: Clinical laboratories throughout England and Wales report results obtained by their own methods. The National Quality Assessment Scheme provides general QA. Statistical significance: $p < 0.05$; chi^2 for trends.

Results: In 1989–94, >10,000 unique patient episodes per year were analysed. In most genera, resistance rates to ampicillin and gentamicin were stable. Overall, imipenem showed least resistance. There were significant trends to increased resistance to ciprofloxacin in *Escherichia, Klebsiella, Enterobacter, Serratia* and *Pseudomonas aeruginosa,* to trimethoprim in *Escherichia, Klebsiella, Enterobacter* and *Serratia,* and to ceftazidime in *Klebsiella* and *Enterobacter.* However, most isolates remained susceptible. In 1994, percentages susceptible to ciprofloxacin were *Escherichia* 98.3, *Klebsiella* 93.5, *Enterobacter* 92.9, *Serratia* 84.8 and *P. aeruginosa* 92.7; to trimethoprim *Escherichia* 75.3, *Klebsiella* 72.9, *Enterobacter* 78.2 and *Serratia* 38.6; and to ceftazidime *Klebsiella* 94.3 and *Enterobacter* 73.5.

Conclusions: Significant trends to resistance have occurred, but absolute resistance rates do not indicate a need for major antibiotic policy changes.

P748 Epidemiological Markers and Aminoglycoside Resistance Mechanisms (AgRM) in Pseudomonas aeruginosa (PA) Multiresistant Strains

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Objective: Multiresistant PA is a major cause of mortality particularly in the immunocompromised host. Similar strains as a rule predominate in several tertiary hospitals. To apply correct hygienic measurement it is very important to clarify if one or several clones are found.

Methods: 22 (8.7%) out of 254 PA strains collected from 35 Greek hospitals, in 1994 were found resistant to all antipseudomonal antibiotics. Serotyping (DIFCO set) and typing by cell envelope proteins (CEPs') study, were performed. Their AgRM's were determined with the AgR phenotypes to 12 Ags.

Results: Among the 22 strains studied the most common serotype was 0_{12} with four different CEPs' profiles. Other predominants serotypes were the 0_{11}, 0_5, 0_1 & 0_2. Five single AgRM occured in 3 combinations. A permeability problem to all Ags was detected in 18 strains while AAC (6′)-II, AAC (3′)-II and APH (3′)-I enzymes were detected in 19 strains, and AAC (3)-I was found in 4 strains. The most common combination was permeability + AAC (3′)-II + AAC (6′)-II + APH (3′)-I (68%). The combination of AAC (3′)-I + AAC (3′)-II + AAC (6′)-II + APH (3′)-I was detected in 4 strains (18%) while permeability was the only cause of resistance in only 3 strains (14%).

Conclusion: The detected Ags mechanisms were similar to those found in previous studies of our group (J Chem 7 (S2): 17, 1995). No correlation between epidemiological typing and AgRM was found.

P749 Proteus and Providencia. Incidence and Antibiotic Sensitivity

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Objectives: To evaluate the species incidence and their sensitivity to the antibiotic of the strains isolated from 1994 to 1996.

Methods: The strains are isolated from patients specimens, identified with the API galleries and their sensitivity tested with the antibiotic diffusion technique.

Results: 453 strains were isolated (439 *Proteus* and 14 *Providencia*). The species incidence is *P. mirabilis* (70.3%, *P. morganii* (16.8%), *P. vulgaris* (6.8%) and *P. rettgeri* (5.9%). The antibiotic sensitivity pattern of proteus genus sic showed resistance of most of the organisms to Ampicilline, Amoxicilline +Clavulanique. Ac, Cefalotine, and gentamycine and sensitivity to Cefotaxime, Netilmycine, Amikacine Pefloxacine. The *providencia* is resistant only to Ampicilline.

Conclusion: *P. mirabilis* is much more frequently isolated from clinical specimens (70.3%) than the other species.

The *providencia* genus is not frequent (only 14 strains were isolated through the three years) and remains sensitive to the antibiotics tested except for ampicilline (85.7% of resistance).

P750 Exclusion of Duplicate Isolates does not Affect Measured Resistance Rates

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Objectives: To assess the effect of exclusion of duplicate isolates on the analysis of antimicrobial susceptibility patterns of micro-organisms from patients in an adult Intensive Care Unit (ICU).

Methods: The resistance patterns, based on disc susceptibility testing, of all bacterial and fungal isolates from routine microbiology samples from patients in ICU were obtained from the Microbiology Laboratory Computer. A computer algorithm was used to exclude duplicate isolates. A duplicate isolate was defined as one of the same species and susceptibility pattern isolated from a single patient within a period of 30 days. Results were compared with and without the exclusion of duplicate isolates. The statistical significance of differences in percentages were assessed by calculation of 95% confidence intervals.

Results: During 1995, 2453 isolates were obtained. Of these, 1093 (45%) were duplicates. Duplicate isolates were more frequent among *Serratia* spp (72%), MRSA (65%), and other *Staph. aureus* (59%) and less frequent among *Steno. maltophilia* (18%), *Acinetobacter* spp (23%). When results for all isolates were compared with those for unique patient isolates no significant difference was observed between any resistance rates, in particular those of gentamicin, azlocillin, imipenem, ceftazidime, ciprofloxacin, amoxycillin and trimethoprim in Gram-negative species, of penicillin, methicillin, gentamicin, vancomycin, rifampicin, and fusidate in Gram-positive species and of fluconazole for *Candida* spp.

Conclusions: Although bacterial species vary in their propensity to persist in patients in our ICU, measured resistance frequencies (for guidance on empirical therapy) are not affected by the exclusion of duplicate isolates.

P751 Selection Pressure of Previous Antibiotherapy and/or Hospitalisation of *Streptococcus pneumoniae* (Sp), *Haemophilus influenzae* (Hi) and *Moraxella Catarrhalis* (Mc) Isolated from Adult Patients with a Lower Respiratory Tract Infection (LRTI), in Europe

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Objective: To investigate the selection pressure of Sp, Hi, Mc isolated in adult community-acquired LRTI.

Methods: A multicenter study was implemented between December 1994 and 1995 in France (F). Germany (D), Great Britain (GB), Hungary (H), Ireland (IRL), Italy (I) the Netherlands (NL), Portugal (P), Slovakia (SK) and Spain (E). The betalactamase production and MICs of penicillin (Pen), erythromycin (Er), tetracycline (Te) and sparfloxacin (Spx) were determined (using cefinase discs (Hi, Mc), agar diffusion E test (H, IRL), agar dilution (GB) and broth microdilution using microplates. Resistant Sp (R-Sp) were defined as non susceptible to Pen and/or Er and/or Te and/or Spx; resistant Hi and Mc (R-Hi, R-Mc) were betalactamase producers and/or non susceptible to Te and/or Er (Mc only). A positive selection pressure (Pr+) was defined by an antibiotic prescription and/or hospitalisation during the month prior to the patient LRTI.

Results: A total of 1872 strains (572 Sp, 991 Hi, 309 Mc) were isolated from acute exacerbation of chronic bronchitis (AECB: 51%), pneumonia (PN: 17%) or chest infection (CI: 32%). No Hi and Mc, and only 5 Sp (0.9%) were resistant to Spx. Resistance was more frequent ($p < 0.05$) in Pr+ strains (in Pr+ Sp, but not in Pr+ Hi and Mc):

	Pr+	Pr−
Sp + Hi + Mcn = 492	n = 1380	
R-Sp + R-Hi + R-mcn = 326	n = 811	

Conclusion: The most significant Pr+ was found with macrolides. Pr+ was between 15% (NL) and 49% (SK), and less frequent in CI (22%) than in AECB and PN (28%).

Malaria

P752 An Open Comparative 28 Day Trial of CGP 56697 (2 Days) versus Oral Quinine (8 Days) in the Treatment of Acute *P. falciparum malaria* in Thai Children

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Treatment groups: 219 children were randomly assigned to oral treatment with **CGP 56697 for 48 hours** (n = 111) or **quinine for 8 days** (n = 108) in three rural centres in Thailand.

Trial population: Children weighing >10 kg with uncomplicated *P. falciparum malaria*. Median baseline parasitaemia was 48,145/μL (Centre 1: 47,550/μL; Centre 2: 89,550/μL; Centre 3: 21,400/μL).